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The concentrations and cumulative risk assessment of phthalates in general population from Shanghai: The comparison between groups with different ages

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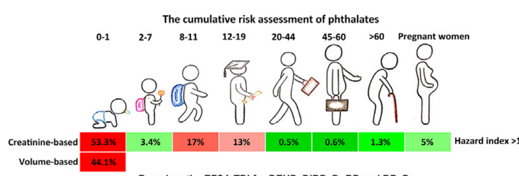
HIGHLIGHTS

- Phthalate exposures were investigated in both general and sensitive populations.
- The exposure was low in adults but presented at a relatively high level in childhood.
- MiBP and MnBP exposures were relatively high in infants and pregnant women.
- The infants were possibly at a high risk of cumulative exposure to phthalates.

GRAPHICAL ABSTRACT



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ABSTRACT

Phthalates are predominantly used as plasticizers in daily consumer products. People are regularly exposed to phthalates through contact with these products. Phthalates are suspected to cause adverse effects in general population. We detected 10 metabolites of 6 phthalates in 3348 urine samples of general population (infants (0–1 yr), children and adolescents (2–19 yr), adults (≥20 yr), and pregnant women) from Shanghai. The Daily intake for phthalates was estimated based on the levels of urinary metabolites. Hazard quotient (HQ) was used to evaluate the risk from the exposure to a single chemical. For the cumulative risk calculation, HQs of different phthalates were added to produce the Hazard index (HI). Overall, exposure was low in adults but presented at a relatively high level throughout childhood. The exposure to some specific phthalates was high in infants and pregnant women. The cumulative risk assessment showed cause for concern mainly for infants and children subgroups. The results indicated that general population from Shanghai was widely exposed to phthalates and the infants were possibly at a high risk of cumulative exposure to phthalates.

1. Introduction

Phthalates are predominantly used as plasticizers in polyvinyl chloride (PVC). Humans are frequently exposed to phthalates due to the wide range use of phthalates-containing products (Gao et al., 2016). U.S. Environmental Protection Agency (EPA) list phthalates as "chemicals of concern", because of their reproductive and

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developmental toxicity (Boberg et al., 2008; Gray Jr. et al., 2006). Pregnant mothers (their embryos) and infants are the most vulnerable populations to phthalate toxicity. Animal and human research has suggested the association of phthalates with preterm birth, low birth weight, and decreased birth length (Toft et al., 2012). Phthalates are also suspected to increase the risk of allergic symptoms and asthma in children (Bornehag et al., 2005; Jaakkola & Knight, 2008), have adverse effect on semen quality in male adults (Joensen et al., 2012; Li et al., 2011), and increase the risk of endometriosis in women (Patel et al., 2015).

To date, an increasing number of human biomonitoring studies have been performed in some countries (e.g., U.S., Germany, Canada, Denmark, Norway, and Belgium). Of special interest, phthalate exposures have been assessed in populations at sensitive periods of human development, including pregnant women, infants, and children. The concentrations of urinary metabolites of phthalates have been indicated to be higher in children and infants than in adults. Infants' and children's physiological changes, developmental stages, and specific behaviors may increase the levels of exposure to phthalates. It is therefore important to understand the exposure levels at different life stages of human beings. However, the available data on phthalate exposure are still not sufficient. This is especially the case in China, where the literature on exposure assessment of phthalate is limited and no reports on infants have been found.

On the other hand, since people are exposed to multiple phthalates simultaneously, it is important to conduct the cumulative risk assessment (CRA) of exposure to phthalates. As U.S. National Research Council recommended, the CRA is based on the common adverse effects resulting from the simultaneous exposure to multiple phthalates and other chemicals (e.g. triclosan, BPA, parabens etc.). The CRA method has been adapted in many studies from different countries (Guo et al., 2011a; Guo et al., 2011b; Han et al., 2013; Pan et al., 2006; Wang et al., 2015); however, the results are inconsistent and the data are still limited due mainly to small sample size and population difference. In China, the literature on CRA is extremely limited, especially for those vulnerable populations. To the best of our knowledge, there was only one CRA study for children, three for pregnant women (Wang et al., 2015; Zhu et al., 2016; Yao et al., 2016), and none for infants. The level of exposure to phthalates in general population from China is largely unknown.

In this study, we aimed to provide a comprehensive evaluation of the exposure to phthalates for general population in Shanghai.

2. Method

2.1. Study populations

Phthalate metabolites were detected in 3348 urine samples including 152 infants (0–1 yr), 387 children and adolescents (2–19 yr), 2355 adults (≥20 yr), and 454 pregnant women. The demographic information for different subpopulations was presented in Table S1. The study populations in this study were from three sources. All study participants from three populations gave their written and informed consent before the investigation. The study was approved by the local authorities and the Ethics Committee of School of Public Health at Fudan University.

2.1.1. General population

One major population in this study came from the Shanghai Food Consumption Survey (SHFCS). We have described the detail of the SHFCS in our previous study (Dong et al., 2017a). Briefly, the SHFCS was conducted four times in a community-based general population from September 2012 to August 2014. A total of 4623 participants from 1760 households were invited to participate the SHFCS in Fall 2012 by answering a questionnaire and leaving a spot urine sample. There were 3322 participants who completed the questionnaire investigation and 3082 provided urine samples. These participants were randomly selected from 25 communities representing 9 districts/counties in Shanghai based on the population density using a multi-stage cluster random sampling method. After the exclusion of participants without enough volume of the urine sample and for unreasonable concentrations of creatinine (<20 μmol/L or > 30,000 μmol/L), 2742 participants with ages ≥2 yr had their phthalate metabolites being measured.

2.1.2. Infants

From March to May 2014, we conducted a pilot investigation on phthalate exposure in infants (0–1 yr). Three of 18 districts/counties in Shanghai were randomly selected, namely Putuo, Jing'an, and Changning. We randomly chose one community hospital from each district/county for recruiting infant volunteers. All these hospitals had their own system of children immunization program. 200 infants aged 0–1 yr during March–May 2014 from the system were invited to participate the investigation, and 154 infants' parents finished the questionnaire investigation and collected urine samples from infants. After the exclusion of two participants with unreasonable concentrations of creatinine, 152 infants were finally assessed in this study.

2.1.3. Pregnant women

From June to September 2013, we conducted a pilot investigation on the relationship between phthalate exposure and birth outcomes in pregnant women. In China, pregnant women were required to attend routine examinations biweekly at the third trimester of pregnancy. We randomly picked two mornings each week during the investigation period. Then, we invited all women at the third trimester of pregnancy to attend the routine examination from an obstetrical and gynecological hospital to participate in our study. The median (Inter Quartile Range) of gestational week for urine sample collection was 39.5 (38.8, 40.3). A total of 545 women were invited, 537 of which left urine samples. Of those 537 women, 83 of them had no measured data of phthalate metabolites because they did not give birth in the hospital or they had a premature delivery. Therefore, the final sample size for pregnant women in this study was 454 cases.

2.2. Assessment of urinary metabolites of phthalates

Urine collection and metabolite measurement was previously described using liquid chromatography tandem mass spectrometry (API 4000, LC-MS/MS, Shimadzu, USA). Details on this methodology have been provided elsewhere (Dong et al., 2017b): "Briefly, 1 mL of urine sample was incubated with β-glucuronidase at 37°C for 120 min. The sample was subsequently acidified with 1 mL of aqueous 2% (v/v) acetic acid, mixed with 100 μL of internal standard (100 μg/L), and loaded into a PLS column previously activated with 2 mL methanol and 2 mL of aqueous 0.5% (v/v) acetic acid. After sample loading, the column was washed with eluted with 1 mL of methanol and 2 mL of aqueous 0.5% (v/v) acetic acid. The eluate was passed through a 0.2-μm filter and analyzed (10 μL) by LC-MS/MS coupled to an AQUASIL C18 column. For the quality control of laboratory procedures, we processed four matrix-spiked samples at two different spiking concentrations (10 and 25 ng/mL) and two procedural blanks in each batch of 30 samples. The average recoveries and relative standard deviations (RSD) of target metabolites in spiked samples ranged from 71.5% to 109.1% and from 1.2% to 7.4% at 10 ng/mL respectively, and ranged from 58.5% to 139.2% and from 0.8% to 8.1% at 25 ng/mL. Trace concentrations of MEP, MnBP, MiBP, and MEHP were detected in procedural blanks with average concentrations and RSDs ranging from 0.05 to 0.8 μg/L and from 3.7% to 9.3%, respectively. Sample concentrations of these metabolites were determined after subtraction of the blank values."

Ten phthalate metabolites were measured in this study, including monomethyl phthalate (MMP), monoethylphthalate (MEP), mono-n-butylphthalate (MnBP), monoisobutylphthalate (MiBP), mono-benzylphthalate (MBzP), mono-2-ethylhexylphthalate (MEHP),